REMARKS/ARGUMENTS

I. Status of Claims and Formal Matters

Claims 1-2, 5-6, 8-15, 18, 25, 28-30, 33 and 36-37 are pending in this application. Claims 3-4, 7, 16-17, 19-24, 26-27, 31-32, 34-35 and 38 were previously canceled. Claims 28-30 and 36-37 are withdrawn. Claims 1, 11 and 12 are proposed to be amended. Upon entry of the proposed amendments, claims 1-2, 5-6, 8-15, 18, 25, 28-30, 33 and 36-37 are pending with claims 1-2, 5-6, 8-15, 18, 25 and 33 under active consideration. Applicant respectfully requests entry of the proposed amendments and remarks into the file history the present application.

Claim 1 is amended to delete the term "prevention"; to specify that the claimed composition(s) are to be administered to a person "with Parkinsonism Plus Syndrome"; to specify that the claimed composition(s) are to be administered in "an effective amount"; to specify that the hGHRH variant has at least "95%" sequence identity to hGHRH; and to delete reference to hGH and hGHRH variants encoded by DNA sequences which hybridize to the complement of the native DNA sequence encoding hGH and hGHRH.

Claims 11 and 12 are amended to specify that the variant is lacking certain amino acids of "hGH."

No new matter is added by the proposed amendments. Paragraph numbers are cited herein with reference to the published application.

II. Patentability Arguments

A. Claim Rejections

1) The Rejections Under 35 U.S.C. § 112, Second Paragraph, Should Be Withdrawn

Claims 1, 2, 5, 6, 8-15, 18, 25 and 33 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner first alleges that claim 1 is indefinite because there is no step indicating that administration of a substance results in treatment of the Parkinson-Plus Syndrome and there is no recitation of a patient population. Applicants herein amend claim 1 to recite that "an effective amount" of the claimed substance(s) is administered, thus clarifying that the claimed substance is administered in an amount effective to treat the Parkinson-Plus Syndrome. With respect to alleged lack of recitation of a patient population, Applicants respectfully disagree. Claim 1 specifies that the claimed substance(s) are to be administered to a person *in need thereof*, thus identifying a specific patient population that is in need of the presently claimed treatment method. Nonetheless, solely to expedite prosecution, Applicants herein amend claim 1 to recite that the claimed substance(s) are to be administered to a person "with Parkinsonism-Plus Syndrome."

The Examiner then alleges that claim 1 is indefinite because the elements in the claim do not constitute proper Markush groups due to the alternative use of "and/or". Applicants herein amend claim 1 to delete reference to the term "or."

The Examiner then alleges that claims 11-12 are indefinite because it is not clear what protein variant the claims are referring to. Applicants herein amend claims 11 and 12 to recite that the variant is "hGH."

In view of the aforementioned amendments, Applicants respectfully submit that all pending claims are in compliance with 35 U.S.C. § 112, second paragraph, and withdrawal of the rejections under this section are hereby requested

2) The Rejections Under 35 U.S.C. 112, First Paragraph (Enablement) Should Be Withdrawn

Claims 1, 2, 6, 8, 10-15, 18, 25 and 33 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. Specifically, the Examiner acknowledges that the specification enables a method for the amelioration of the symptoms of Multiple Symptom Atrophy (MSA) comprising administering to a person suffering from MSA a substance consisting of (a) human growth hormone (hGH), (b) a variant of (a) that has at least 70% sequence identity thereto and that has agonistic activity on the hGH receptor, (c) a salt of (a) or (b), wherein administration of said substance ameliorates the symptoms of MSA. Applicants thank the Examiner for acknowledging that the subject matter of claim 1(a)-(c) is enabled. However, the Examiner alleges that the specification does not enable certain aspects of the presently claimed methods.

First, the Examiner alleges that the specification does not enable the "prevention" of MSA. While strongly disagreeing with the Examiner's analysis and conclusion, Applicants herein amend claim 1 to delete this term from the claim solely to expedite prosecution of the present application.

Second, with respect to (1) hGH or hGHRH variants encoded by DNA sequences which hybridize to the complement of the native DNA sequence encoding hGH and hGHRH and (2) variants of hGHRH at least 70% identical to hGHRH, the Examiner alleges that it would require undue experimentation to make and test every possible variation of the invention for its ability to agonize hGH or hGHRH receptors. Applicants herein amend claim 1 to delete reference to hGH or hGHRH variants encoded by DNA sequences which hybridize to the complement of the

native DNA sequence encoding hGH and hGHRH. Applicants also amend claim 1 to recite that variants of hGHRH have at least "95% sequence identity thereto" and have agonistic activity on the hGHRH receptor. Accordingly, the rejections under 35 U.S.C. 112, first paragraph, directed to sequence less than 95% identical to hGHRH and to sequence encoded by DNA sequences which hybridize to the complement of the native DNA sequence encoding hGH and hGHRH are rendered moot. With respect to variants of hGHRH at least 95% identical to hGRH and having agonistic activity, Applicants respectfully traverse.

Applicants note that the claims do not require that the variants used in the claimed method have exactly the same biological activity as hGHRH (or hGH); rather, the variants used in the claimed method have agonistic activity. In this regard, the Patent and Trademark Office Board of Patent Appeals and Interferences has stated: "The test [for enablement] is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed". *Ex parte Jackson*, 217 U.S.P.Q. 804, 807 (1982); *see also Ex parte Erlich* 3 U.S.P.Q.2d 1011 (B.P.A.I. 1982) (observing that although a method might be "tedious and laborious," such experimentation is nevertheless "routine" defining "routine" experiments as those which use known methods in combination with the variables taught in the patent to achieve the expected, specific, patented result). Applicants believe that the quantity of experimentation is not undue in this matter, as the experimentation required is "routine", utilizing known methods to test for agonistic activity. The present specification provides detailed guidance in the preparation and identification of sequence falling within the scope of the pending claims. For example, the present specification provides guidance to those skilled in the art as to the portions of hGHRH (and hGH) that should be relatively tolerant of amino acid substitutions and those portions where some degree of caution should be exercised in making substitutions (*see*, e.g. paragraphs (0086)-(0111), particularly

paragraphs (0105)-(0106) describing a wide variety of hGH variants with agonistic activity known in the art and paragraphs (0132)-(0133) describing a wide variety of hGHRH variants with agonistic activity). Moreover, hGHRH (and hGH) were well characterized in the art as of the present priority date, as described in the *Background* section of the present specification, and the claimed hGHRH variants share a significant degree of partial structure (i.e. at least 95% of hGHRH). Accordingly, we believe that the application as filed enables the invention as presently claimed

3) The Rejections Under 35 U.S.C. 112, First Paragraph (Written Description) Should Be Withdrawn

Claims 1, 2, 6, 8, 10-15, 18, 25 and 33 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. Specifically, the Examiner states that only isolated polypeptides comprising (a) human growth hormone (hGH) or human growth hormone releasing hormone (hGHRH) (b) a variant of (a) that has at least 70% sequence identity thereto and that has agonistic activity on the hGH or hGHRH receptors, respectively and (c) a salt of (a) or (b) are adequately described the specification. Applicants thank the Examiner for acknowledging that this portion of the subject matter of claim 1 is adequately described by the specification. Applicants herein amend claim 1 to delete reference to hGH or hGHRH variants encoded by DNA sequences which hybridize to the complement of the native DNA sequence encoding hGH and hGHRH. Applicants also amend claim 1 to recite that variants of hGHRH have at least "95% sequence identity thereto" and have agonistic activity on the hGHRH receptor. Accordingly, the rejections under 35 U.S.C. 112, first paragraph, directed to sequence less than 95% identical to hGHRH and to sequence encoded by DNA sequences which hybridize to the complement of the native DNA sequence encoding hGH and hGHRH are rendered moot.

Applicants believe that the claims as presently amended are fully compliant with the written description requirement and therefore withdrawal of the rejections under this section is hereby requested

4) The Rejections Under 35 U.S.C. 102 Should Be Withdrawn

Claims 1, 2, 5, 6, 8, 14, 15, 18, 25 and 33 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Ng et al. (US Patent No. 5,869,452) (hereinafter, the '452 patent). According to the Examiner, the '452 patent teaches administration of GH or a variant of GH containing amino acid residues 177-191 for the treatment of obesity, thus meeting the limitations of claims 1, 5 and 8. Applicants respectfully traverse the rejections and request reconsideration in view of the amendments proposed herein and the following comments:

As discussed above, the recitation in claim 1 that administration of GH is to a "person in need thereof" requires that the claimed composition(s) be administered to a specific subset of the population – namely, those that are identified as being in need of treatment for Parkinsonism-Plus Syndrome. Nonetheless, solely in the interest of expediting prosecution and in no way acknowledging agreement with the Examiner, Applicants herein amend claim 1 to recite that the claimed composition(s) are to be administered to a person "with Parkinsonism-Plus Syndrome." Because the '452 patent fails to describe administration of GH to such a population, the present claims cannot be anticipated by the '452 patent. Applicants thus respectfully request withdrawal of the rejections of claims 1, 2, 5, 6, 8, 14, 15, 18, 25 and 33 under 35 U.S.C. § 102(b) as allegedly anticipated by the '452 patent.

Claims 1, 2, 5, 6, 8, 10, 11, 12, 13, 15, and 18 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Bengtsson et al. (U.S. Patent No. 5,736,515 (hereinafter the '515 patent)) as evidenced by Bauman (Endocrine Reviews, 1991; 12:424-449). The Examiner has construed claim 1 as covering administration of GH to anyone for any reason. Applicants

respectfully traverse the rejections and request reconsideration in view of the amendments proposed herein and the following comments:

As discussed above, this is a misconstruction of claim 1 as previously pending. Nonetheless, Applicants' have amended claim to recite that the claimed composition(s) are to be administered to a person "with Parkinsonism-Plus Syndrome." The pending claims, as amended herein, require that the composition be administered to men who have a recognized diagnosis of Parkinsonism-Plus Syndrome. Administration of GH to persons who do not have a recognized diagnosis of Parkinsonism-Plus Syndrome does not anticipate claim 1 or its dependents. See, e.g. *In re Schreiber*, 128 F.3d 1473, 1477 (to anticipate a claim, a prior art reference must disclose every limitation of the claimed invention, either explicitly or inherently). The '515 patent describes a study in which 20 patients having adult-onset pituitary insufficiency after insulin-induced hypoglycaemia (with serum GH concentration below 5 mU/L) were treated with rhGH. See '515 patent, col. 2, lines 20-67. The '515 patent does not teach or suggest administration of GH to the specifically claimed patient population and does not teach that administration of GH to persons with Parkinsonism Plus Syndrome would be successful in treating the disease. The portion of the '515 patent cited by the Examiner (col. 2, lines 7-11) provides nothing more than speculation that GH could be used to treat "damages in the brain…damages in the memory function of the brain and degenerative disorders of the brain." Such a generic disclosure that GH could be used to treat a genus of brain disorders under which countless specific disorders fall, none of which are specifically identified, does not meet the requirement that the '515 patent specifically describe the claimed invention. Because the '515 patent fails to teach or suggest administration of GH to patients with a recognized diagnosis of Parkinsonism-Plus Syndrome, the '515 patent cannot anticipate the present claims. Thus, Applicants respectfully request withdrawal of the rejection of claims 1, 2, 5, 6, 8, 10, 11, 12, 13, 15 and 18 under 35 U.S.C. § 102(b) as allegedly anticipated by the '452 patent.

Claims 1, 2, 5, 6, 8, 10-15 and 18 stand rejected under 35 U.S.C. § 102(e) as allegedly anticipated by Johannsson et al. (US Patent No. 6,846,800, hereinafter the '800 patent). The Examiner has construed claim 1 as covering administration of GH to anyone for any reason. Applicants respectfully traverse the rejections and request reconsideration in view of the amendments proposed herein and the following comments:

As discussed above, the Examiner has misconstrued claim 1 as previously pending. Nonetheless, Applicants' have amended claim to recite that the claimed composition(s) are to be administered to a person "with Parkinsonism-Plus Syndrome." Because the '800 patent fails to teach or suggest administration of GH to the specifically claimed patient population, the '800 patent cannot anticipate the present claims. Thus, Applicants respectfully request withdrawal of the rejection of claims 1, 2, 5, 6, 8, 10-15 and 18 under 35 U.S.C. § 102(e) as allegedly anticipated by the '452 patent

5) <u>The Rejections Under 35 U.S.C. 103 Should Be Withdrawn</u>

Claim 9 stands rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over the '452 patent as applied to claims 1, 2, 5, 6, 8, 14, 15, 18, 25 and 33 in view of Goeddel et al. (Nature, 1979; 218:544-548 (hereinafter Goeddel). The Examiner characterizes Goeddel as showing how to make methionyl GH and alleges that it would have been obvious to modify the teachings of the '452 patent by making methionyl GH.

Applicants traverse the rejection and request reconsideration because, as discussed above, the '452 patent is fatally defective as an anticipatory reference for the presently claimed invention. Because the '452 patent is not a proper reference under § 102(b), the '452 patent cannot serve as a proper basis for rejections under 35 U.S.C. § 103 even when combined with Goeddel, because Goeddel fails to remedy all of the infirmities of the '452 patent. Accordingly, Applicants respectfully request withdrawal of the rejection of claim 9 over the '452 patent in view of Goeddel.

Claim 9 stands rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over the '515 patent as evidenced by Bauman as applied to claims 1, 2, 5, 6, 8, 10-13, 15 and 18 in view of Goeddel. The Examiner characterizes Goeddel as showing how to make methionyl GH and alleges that it would have been obvious to modify the teachings of the '515 patent by making methionyl GH.

Applicants traverse the rejection and request reconsideration because, as discussed above, the '515 patent is fatally defective as an anticipatory reference for the presently claimed invention. Because the '515 patent is not a proper reference under § 102(b), the '515 patent cannot serve as a proper basis for rejections under 35 U.S.C. § 103 even when combined with Goeddel, because Goeddel fails to remedy all of the infirmities of the '515 patent. Accordingly, Applicants respectfully request withdrawal of the rejection of claim 9 over the '515 patent in view of Goeddel.

6) The Rejections for Nonstatutory Obviousness-Type Double Patenting Should be Withdrawn

Claims 1, 2, 5, 6, 8-15, 18, and 33 stand rejected as allegedly unpatentable over the '515 patent in view of Bauman and further in view of Goeddel on the ground of nonstatutory obviousness-type double patenting. Applicants respectfully traverse the rejection based on the amendments proposed herein and on the following arguments.

As discussed above, the '515 patent is fatally defective as an anticipatory reference for the presently claimed invention. Because the '515 patent is not a proper reference under § 102(b), the '515 patent cannot serve as a proper basis for rejections on the ground of nonstatutory obviousness-type double patenting even when combined with Bauman and/or Goeddel, because neither Bauman nor Goeddel remedies all of the infirmities of the '515 patent. Accordingly, Applicants respectfully request the Examiner withdraw the rejection of claims 1, 2, 5, 6, 8-15, 18, and 33 for nonstatutory obviousness-type double patenting.

CONCLUSION.

Applicants respectfully submit that the instant application is in good and proper order for allowance and early notification to this effect is solicited. The Examiner is hereby respectfully invited to contact the undersigned attorney at the telephone number listed below with any questions, comments, or suggestions relating to this application that may advance this application to allowance.

Respectfully submitted,

HOWREY LLP

Dated: August 27, 2009

By: /David W. Clough /
David W. Clough, Ph.D.
Registration No.: 36,107
Customer No.: 22930
Telephone No.: (312) 595-1408

HOWREY LLP
ATTN: Docketing Department
2941 Fairview Park Drive, Suite 200
Falls Church, VA 22042-9922
Facsimile No.: (703) 336-6950